10/525,290

Uploading C:\Program Files\Stnexp\Queries\JP-103.str

L1 STRUCTURE UPLOADED

=> D L1
L1 HAS NO ANSWERS
L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> S L1 FULL
FULL SEARCH INITIATED 14:45:09 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 76673 TO ITERATE

100.0% PROCESSED 76673 ITERATIONS 9 ANSWERS
SEARCH TIME: 00.00.05

L2 9 SEA SSS FUL L1

=> FILE CAPLUS

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	172.55	172.76

FILE 'CAPLUS' ENTERED AT 14:45:26 ON 30 MAR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 30 Mar 2007 VOL 146 ISS 15
FILE LAST UPDATED: 29 Mar 2007 (20070329/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> S L2
L3 3 L2

=> D L3 IBIB ABS HITSTR 1-3

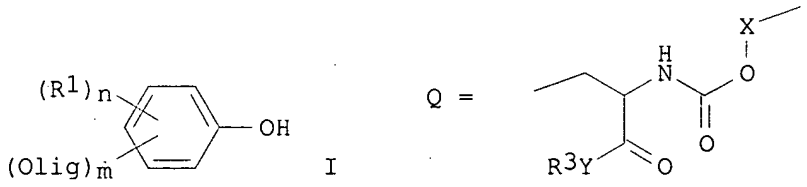
L3 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:158500 CAPLUS
DOCUMENT NUMBER: 142:261295
TITLE: Preparation of aryl carbamate oligomers for hydrolyzable prodrugs and prodrugs comprising same
INVENTOR(S): Ekwuribe, Nnochiri N.; Odenbaugh, Amy L.
PATENT ASSIGNEE(S): Nobex Corporation, USA
SOURCE: PCT Int. Appl., 59 pp.

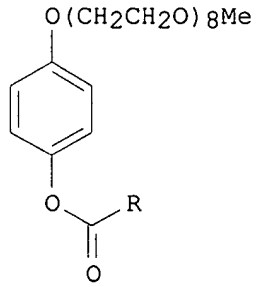
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005016240	A2	20050224	WO 2004-US15004	20040506
WO 2005016240	A3	20060928		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004264818	A1	20050224	AU 2004-264818	20040506
CA 2534298	A1	20050224	CA 2004-2534298	20040506
EP 1651163	A2	20060503	EP 2004-752108	20040506
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
US 2006167234	A1	20060727	US 2005-525290	20050718

PRIORITY APPLN. INFO.:	US 2003-491751P	P	20030801
	WO 2004-US15004	W	20040506

OTHER SOURCE(S): CASREACT 142:261295; MARPAT 142:261295
GI





II

AB The present invention provides a compound having a formula: I [R1 = alkyl, -CH2(OC2H4)OMe, and (OC2H4)OCH3; n = 0-4; Olig = L-O-PAG-(R2)q; L = optional linker moiety CH2O, CH2OX, OX, CO, COX, NH, NHCO, XNHCO, NHCOX, CONH, CONHX, group Q; X = C1-6 alkyl, bond; Y = N, O, bond; R3 = C1-6

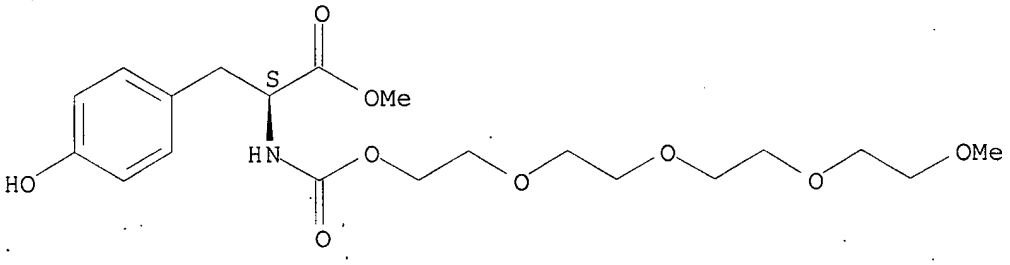
alkyl; PAG = linear or branched polyalkylene glycol moiety; R2 = C1-22 alkyl capping moiety if X is present or C2-22 alkyl capping moiety if X is not present; q = 1 to maximum number of branches on PAG; m = 1-5]. Thus, reaction of oligoethylene glycol mesylate MeSO2O(CH2CH2O)4Me with 4-benzyloxyphenol, followed by hydrogenolysis of the benzyl group, activation with 4-nitrophenyl chloroformate, and reaction with leucine-enkephalin or human insulin gave prodrugs II (R = leucine enkephalin or insulin residue). Hydrolysis studies of the prepared prodrugs by carboxylesterase and in rat plasma are given.

IT 845910-83-0DP, tyrosine side chain conjugates with human insulin
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aryl carbamate oligomers for hydrolyzable prodrugs and prodrugs comprising same)

RN 845910-83-0 CAPLUS

CN 2,5,8,11,14-Pentaoxa-16-azaoctadecan-18-oic acid, 17-[(4-hydroxyphenyl)methyl]-15-oxo-, methyl ester, (17S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

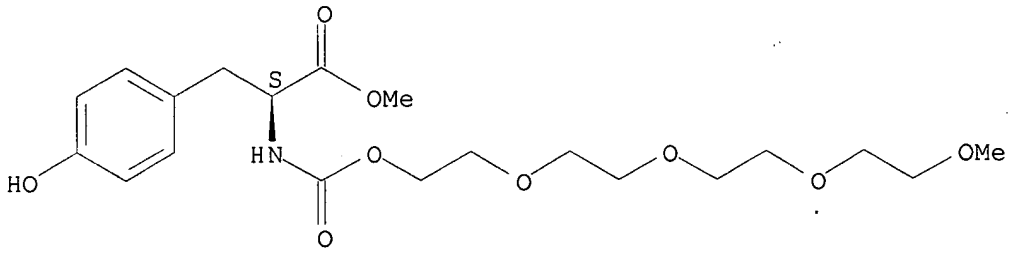


IT 845910-83-0P 845910-87-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aryl carbamate oligomers for hydrolyzable prodrugs and prodrugs comprising same)

RN 845910-83-0 CAPLUS

CN 2,5,8,11,14-Pentaoxa-16-azaoctadecan-18-oic acid, 17-[(4-hydroxyphenyl)methyl]-15-oxo-, methyl ester, (17S)- (9CI) (CA INDEX NAME)

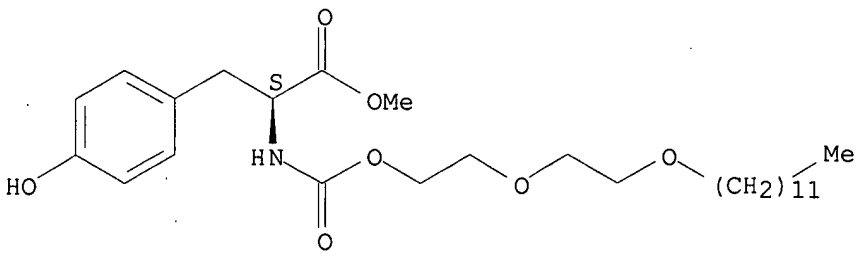
Absolute stereochemistry.



RN 845910-87-4 CAPLUS

CN 5,8,11-Trioxa-3-azatricosanoic acid, 2-[(4-hydroxyphenyl)methyl]-4-oxo-, methyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:380315 CAPLUS
DOCUMENT NUMBER: 131:144830
TITLE: Synthesis and evaluation of the physicochemical properties of esterase-sensitive cyclic prodrugs of opioid peptides using an (acyloxy)alkoxy linker
AUTHOR(S): Bak, A.; Siahaan, T. J.; Gudmundsson, O. S.; Gangwar, S.; Friis, G. J.; Borchardt, R. T.
CORPORATE SOURCE: Department of Analytical and Pharmaceutical Chemistry, The Royal Danish School of Pharmacy, Copenhagen, DK-2100, Den.
SOURCE: Journal of Peptide Research (1999), 53(4), 393-402
CODEN: JPERFA; ISSN: 1397-002X
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

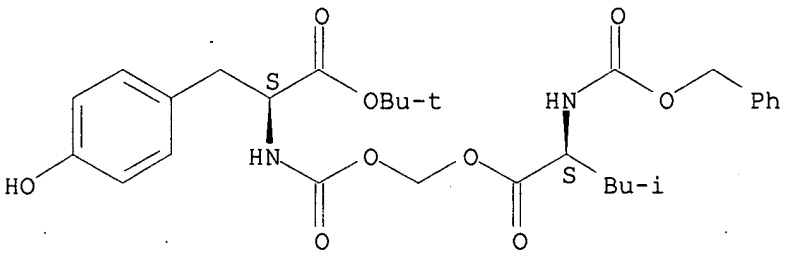
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The objective of this work was to synthesize the cyclic prodrugs I and II of [Leu5]-enkephalin (H-Tyr-Gly-Gly-Phe-Leu-OH) and DADLE (H-Tyr-D-Ala-Gly-Phe-D-Leu-OH), resp., using an (acyloxy)alkoxy linker. The cyclic prodrugs I and II were synthesized via a convergent method using the (acyloxy)alkoxy pro-moiety that connected the C- and N-terminus of the peptides. The cyclic prodrugs I and II exhibited Stokes-Einstein mol. radii similar to those of [Leu5]-enkephalin and DADLE; however, the cyclic prodrugs were shown to be significantly more lipophilic than the corresponding opioid peptides, as determined by partitioning expts. using immobilized artificial membrane (IAM) column chromatog. In addition, the cyclic prodrugs exhibit stable solution conformations, which reduce their hydrogen bonding potentials. Based on these physicochem. characteristics, the cyclic prodrugs I and II should have exhibited better transcellular flux across the Caco-2 cell monolayer than [Leu5]-enkephalin and DADLE, resp. However, the cyclic prodrugs I and II were shown in sep. studies to be substrates for P-glycoprotein, which significantly reduced their ability to permeate across Caco-2 cell monolayers. When P-glycoprotein was inhibited, the permeability characteristics of prodrugs I and II were consistent with their physicochem. properties.

IT 236426-31-6P 236426-32-7P 236426-33-8P
236426-34-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and peptide delivery activity of (acyloxy)alkoxy-containing cyclic prodrugs of opioid peptides)

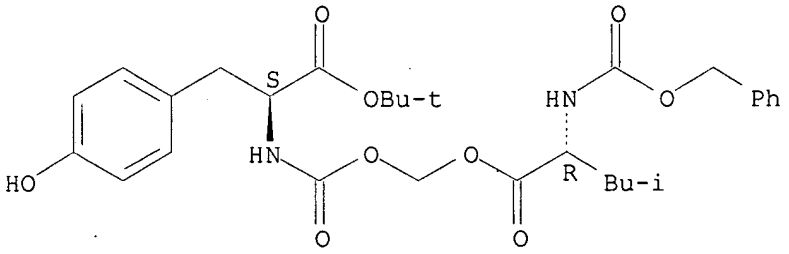
RN 236426-31-6 CAPLUS
CN L-Tyrosine, N-[(hydroxymethoxy)carbonyl]-, 1,1-dimethylethyl ester, α-ester with N-[(phenylmethoxy)carbonyl]-L-leucine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



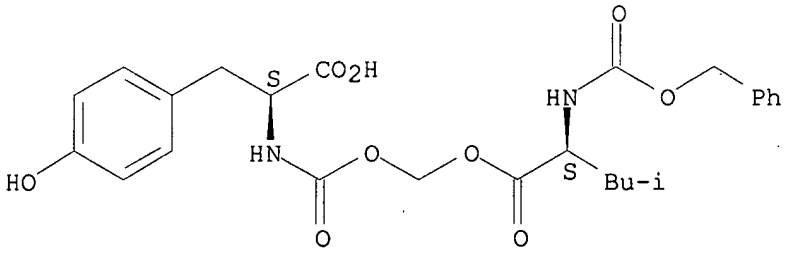
RN 236426-32-7 CAPLUS
CN L-Tyrosine, N-[(hydroxymethoxy)carbonyl]-, 1,1-dimethylethyl ester, α-ester with N-[(phenylmethoxy)carbonyl]-D-leucine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



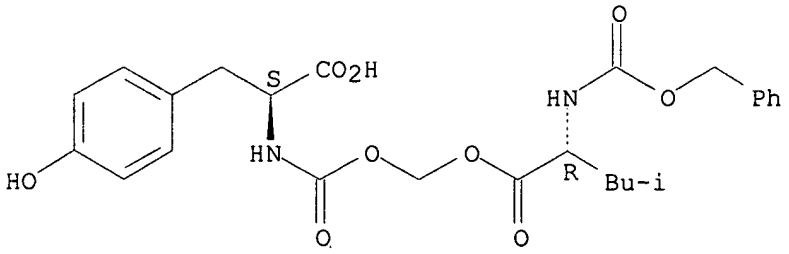
RN 236426-33-8 CAPLUS
CN L-Tyrosine, N-[(hydroxymethoxy)carbonyl]-, α-ester with N-[(phenylmethoxy)carbonyl]-L-leucine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



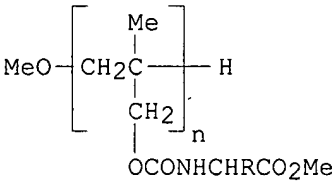
RN 236426-34-9 CAPLUS
CN L-Tyrosine, N-[(hydroxymethoxy)carbonyl]-, α-ester with N-[(phenylmethoxy)carbonyl]-D-leucine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

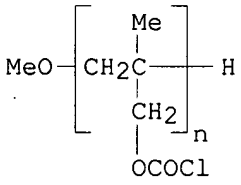


REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:207623 CAPLUS
DOCUMENT NUMBER: 104:207623
TITLE: Fixation of trifunctional amino acids on oligomethacrylic supports. Tyrosine and glutamic acid
AUTHOR(S): Laguerre, A.; Rabadeux, J. C.; Gueniffey, H.; Bruneau, C. M.
CORPORATE SOURCE: Fac. Sci., Univ. Maine, Le Mans, 72017, Fr.
SOURCE: European Polymer Journal (1985), 21(7), 619-22
CODEN: EUPJAG; ISSN: 0014-3057
DOCUMENT TYPE: Journal
LANGUAGE: French
GI



I



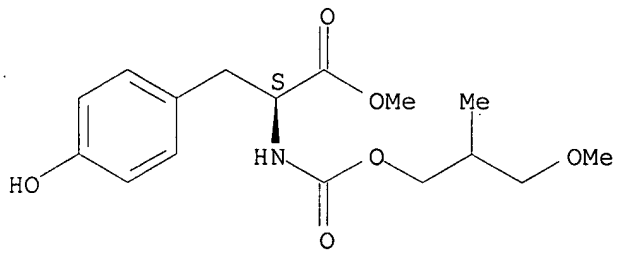
II

AB Tyrosine and glutamic acid were fixed by their NH2 groups onto oligomethacrylic supports through a urethane function. Polyfunctional products able to act as precursors for networks are obtained. Thus, fixation products I (R = CH2C6H4OH-p, CH2CH2CO2Me; n = 1, 2, 3) were prepared by treating chloroformates II with H2NCHRCO2Me.

IT 102039-89-4P 102039-90-7P 102059-99-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

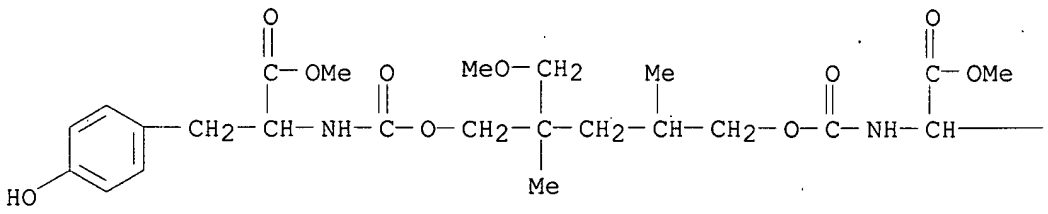
RN 102039-89-4 CAPLUS
CN L-Tyrosine, N-[(3-methoxy-2-methylpropoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

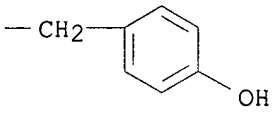


RN 102039-90-7 CAPLUS
CN 5,11-Dioxa-3,13-diazapentadecanedioic acid, 2,14-bis[(4-hydroxyphenyl)methyl]-7-(methoxymethyl)-7,9-dimethyl-4,12-dioxo-, dimethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

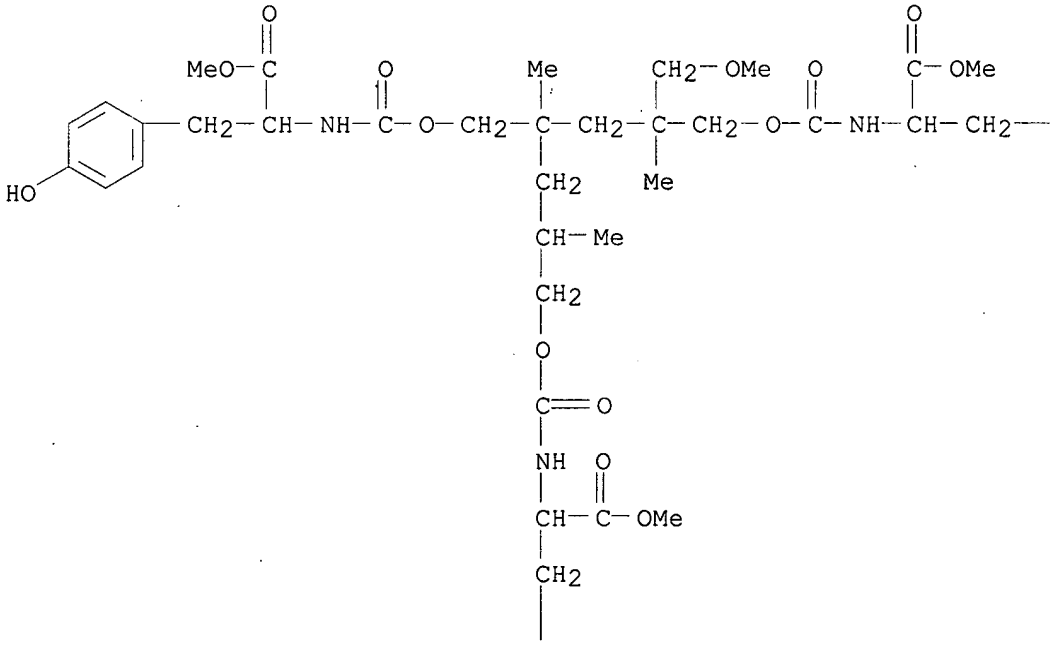


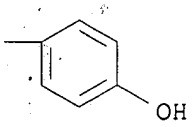
PAGE 1-B



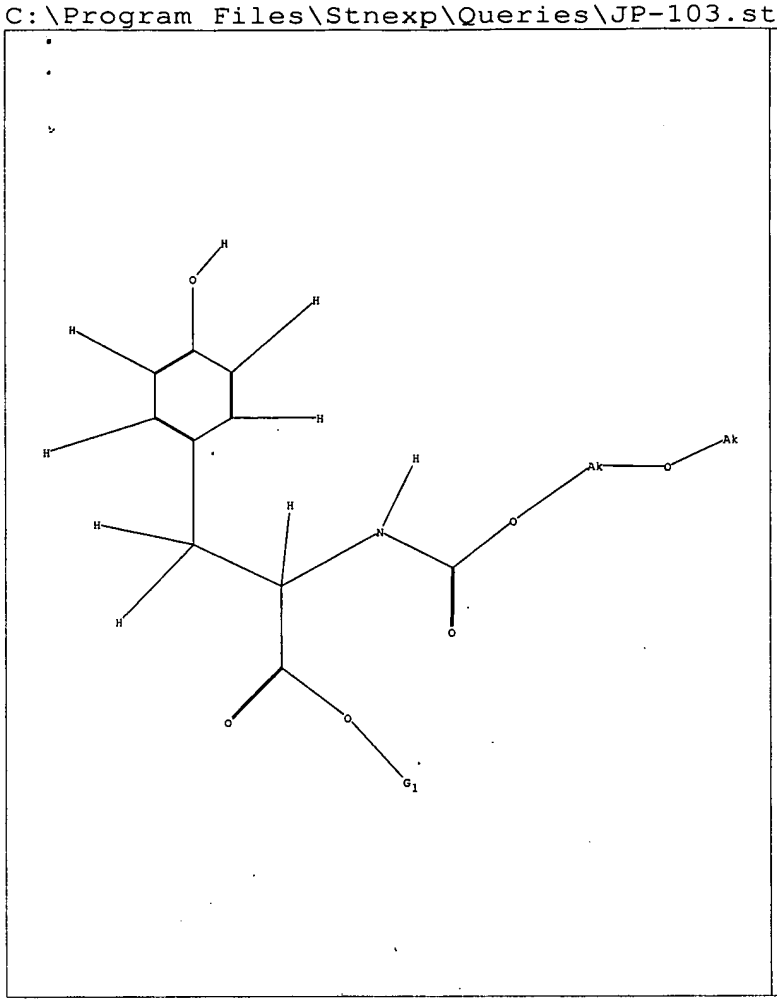
RN 102059-99-4 CAPLUS
CN 5,13-Dioxa-3,15-diazaheptadecanedioic acid, 2,16-bis[(4-hydroxyphenyl)methyl]-9-[[[[[1-[(4-hydroxyphenyl)methyl]-2-methoxy-2-oxoethyl]amino]carbonyl]oxy]methyl]-7-(methoxymethyl)-7,9,11-trimethyl-4,14-dioxo-, dimethyl ester (9CI) (CA INDEX NAME)

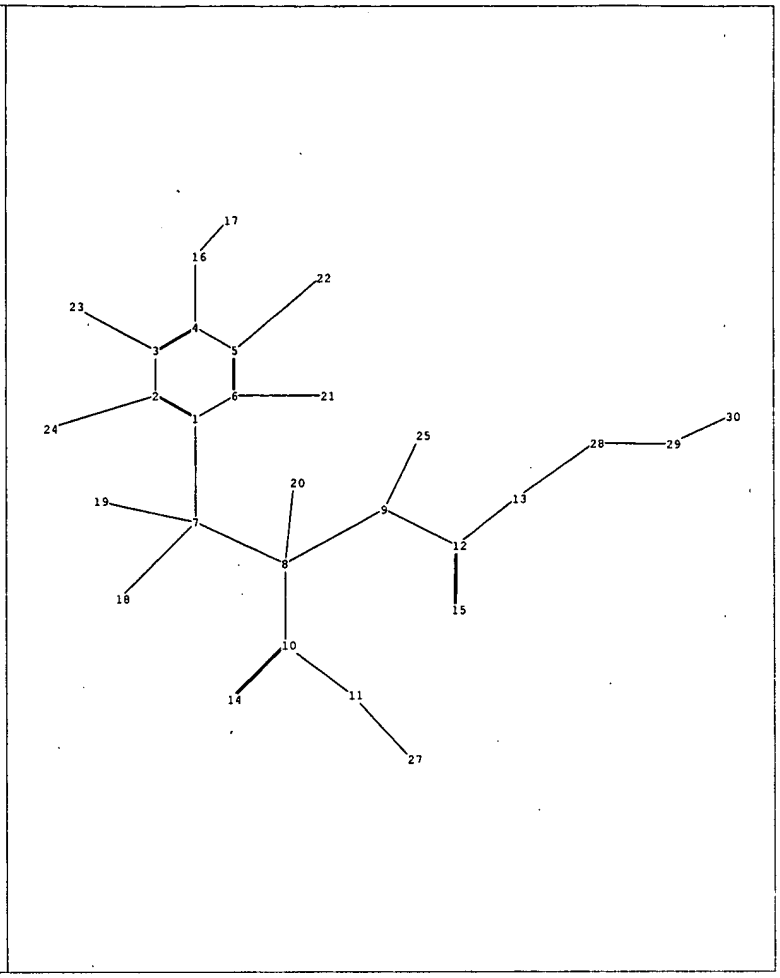
PAGE 1-A




OH

C:\Program Files\Stnexp\Queries\JP-103.str





chain nodes :
7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 27 28 29 30
ring nodes :
1 2 3 4 5 6
chain bonds :
1-7 2-24 3-23 4-16 5-22 6-21 7-8 7-18 7-19 8-9 8-10 8-20 9-12 9-25 10-11 10-14 11-27 12-13 12-15 13-28 16-17 28-29 29-30
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
4-16 8-9 9-12 10-11 10-14 11-27 12-13 12-15 13-28 28-29 29-30
exact bonds :
1-7 2-24 3-23 5-22 6-21 7-8 7-18 7-19 8-10 8-20 9-25 16-17
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

G1:H,Ak

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS